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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,612	05/14/2001	Thomas Spies	FHCC:003USC1	9260

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EXAMINER

VANDERVEGT, FRANCOIS P

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/855,612

Applicant(s)

SPIES ET AL.

Examiner

F. Pierre VanderVegt

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 23 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

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### DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 09/303,161.

Claims 26-101 have been canceled.

Claims 1-25 are currently pending and are the subject of examination in the present Office Action.

Applicant is reminded of the responsibility to list the status of ALL claims that are currently or formerly pending in an application. Applicant is also reminded that only the officially recognized status identifiers should be used.

#### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 14, 2004 has been entered.

#### *Priority*

2. The first paragraph of page 1 of the instant specification states that:

"The present application is a continuation-in-part of co-pending U.S. Provisional Patent Application Serial No. 60/029,044 filed October 29, 1996. The entire text of the above-referenced disclosure is specifically incorporated by reference herein without disclaimer. The present application is also a continuation of U.S. Serial No. 09/303,161, filed April 29, 1999, and PCT/US97/20170, filed October 29, 1997."

However, the instant application was filed on May 14, 2001 and therefore was never co-pending with the 60/029,044 provisional application, which expired October 29, 1997 and cannot claim direct priority to the provisional. Furthermore, it is not proper to term a non-provisional application as a Continuation-in-Part of a provisional application. The only priority application that can claim priority to the '044 provisional application is PCT/US97/20170.

In addition, the instant application cannot be a direct "continuation" of PCT/US97/20170, because the PCT application expired on April 29, 1999 and the instant application was therefore never co-pending with the PCT application either.

Applicant should therefore amend the first paragraph of the specification to correctly reflect the priority information. For example, --This application is a continuation of U.S. Application Serial Number

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09/303,161, which is a continuation of Application Serial Number PCT/US97/20170, which claims the benefit of the filing date of provisional application 60/029,044.--

*Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Briefly, claims 1-25 have been amended to recite a method of "screening for potential carcinogenesis in a patient" comprising providing a sample from the patient and identifying MICA or MICB expression in the sample.

Claims 22-23 recite a number of different sources of sample tissues.

Claims 24-25 recite a number of different potential carcinoma types, but are not related to the source of the tissue sample.

The specification discloses on page 9 that the "inventors have shown that MICA is expressed in various cancer cell lines suggesting that cells may be screened for the **overexpression** of MICA and/or MICB, its presence indicating potential carcinogenesis" (emphasis added for clarity). The specification further discloses that the "expression of MICA in tumor cells provides a marker for diagnostic screening methods for cancer in, for example, tumor or tissue biopsy samples" (page 10, lines 4-5), and that "MICA and/or MICB expression in tumor cells may be detected" (page 10, lines 5-6). The specification also discloses on page 75, lines 1-9 that MICA was detected on tumor cell lines HT29 (colon carcinoma) and U373 (astrocytoma).

However, the specification does not disclose how to correlate the identification of MICA/B expression in a sample to the potential of carcinogenesis versus the level of MICA/B expression in normal tissue or due to other factors. As stated in previous actions, Groh et al (PNAS 93:12445-12450; of record) teaches that MICA and MICB are normally expressed in the gastrointestinal epithelium but does not indicate expression associated with cancer cells (see entire article, Abstract in particular). Groh et al (Science 1998 279:1737-1740; of record) discloses expression of MICA/B is stress related and may be

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indicative of damaged, infected or transformed intestinal epithelial cells (see entire report, page 1740 in particular). Applicant's specification at page 9 clearly recognizes that the relationship of MICA/B expression to potential carcinogenesis in a patient is related to an "overexpression" of MICA/B in a sample. However, the specification does not teach the level of overexpression that is indicative of potential carcinogenesis. There is no teaching in the specification or claims as originally filed of any method that correlates MICA/B expression levels to potential carcinogenesis. Mere detection of MICA and/or MICB in a tissue sample is insufficient as an indicator of potential carcinogenesis in the subject from whom the sample is obtained. At what point does MICA and MICB detection in the tissue become indicative of cancer? If indicators that are present in normal tissue are to be used as an indicator of diseased, cancerous tissue, there must exist a means for differentiating the expression of those indicators in the cancerous tissue from the expression of those indicators in the normal tissue.

Furthermore, there is no correlation in the claimed method between the type of potential carcinogenesis in the patient and the source tissue for the patient sample or for the type of tumor. There is no guidance in the claims or specification regarding the relationship of the type of tissue sample tested and the patient tissue in which a potential carcinogenesis may be present. Groh et al (Proc. Nat. Acad. Sci. (USA) [1999] 96:6879-6884; U2 on form PTO-892) discloses that MICA/B expression is associated with epithelial tumors, irrespective of the tissue type (Abstract, first column of page 6883 and Figure 4 in particular). However, the instant claims are broadly drawn to the detection of "potential carcinogenesis in a patient" without regard to the tumor (or cancerous cell) type. The state of the art only recognizes that MICA/B is overexpressed in tumors of epithelial cells and the instant specification does not provide any evidence or teaching that would lead the artisan to predict that detection of MICA/B expression could be indicative of any other type of tumor.

The instant disclosure provides limited guidance in the specification regarding a method for the artisan to detect potential carcinogenesis in a patient comprising identifying expression of MICA or MICB in a sample from that patient without correlation of that expression level to the expression level in normal tissue or samples that may exhibit stress induced expression of MICA and/or MICB. The instant disclosure provides no guidance in the specification regarding a method for the artisan to detect potential carcinogenesis in a patient comprising identifying expression of MICA or MICB in a sample from that patient when the tissue being sampled is different from the tissue of the patient that is potentially cancerous.

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Given the limited working examples in the specification, the state of the art at the time the invention was made and the level of guidance required to practice the claimed invention, it would require undue experimentation for one of skill to practice the claimed invention.

*Conclusion*

4. No claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D. *RV*  
Patent Examiner  
December 9, 2004

*Pat J. Nolan*  
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PRIMARY EXAMINER  
*12/13/04*